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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/270,983	03/17/1999	BRUCE A. HAY	CIT1130-1	3362

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	23

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/270,983	HAY ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,57 and 58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,57 and 58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 November 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants amendment of the specification, amendment of claim 1 and addition of new claims 57 and 58, Paper No. 20, 11/21/2002 and Paper No. 22, 11/25/2002, is acknowledged.

Claims 1-8, 57 and 58 are at issue and are present for examination.

Applicants' arguments filed on 11/25/2002, Paper No. 22, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Drawings

The newly submitted drawings, Paper No. 20, 11/21/2002, are objected to for the reasons stated on the enclosed form PTO-948.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8, 57 and 58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (2-8, 57 and 58 dependent from) is indefinite in that it is drawn to a fusion protein comprising a reporter polypeptide linked through a linker polypeptide to a repressor polypeptide, wherein said reporter can be a "polypeptide having an epitope that can be bound by an antibody or active antibody fragment" and the repressor polypeptide "represses the activity of the reporter polypeptide by conferring a specific localization in a cell such that the reporter polypeptide has reduced activity." The above quoted limitations of said reporter polypeptide and said repressor polypeptide are unclear. First, it should be noted that most polypeptides have an epitope that can be bound by an antibody or active antibody fragment, and thus this limitation of the referred to reporter polypeptide is extremely broad encompassing most polypeptides. Second, as the repressor polypeptide represses the "activity" of the reporter polypeptide, the referred to "activity" is unclear since this refers to the "activity" of a reporter that encompasses most polypeptides. What "activity" are applicants referring to that is encompassed by most polypeptides? If one assumes that the "activity" that applicants are here referring to is the "ability to be bound by an antibody or active antibody fragment", then it is unclear how such an activity can be repressed by "conferring a specific localization in a cell such that the reporter polypeptide has reduced activity".

Claim 58 recites the limitation "the inhibitor polypeptide" in claim 1. There is insufficient antecedent basis for this limitation in the claim. It is believed that applicants intent was to refer to the repressor polypeptide.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicants amendment of the claims and traversal of the earlier 112 first paragraph rejections is acknowledged, as the previous rejections were based on the lack of written description and a lack of an enabling disclosure of the full scope of those fusion proteins comprising any repressor protein. The 112 first paragraph rejections below, necessitated by applicants amendment, are based on the lack of written description and lack of an enabling disclosure for the claimed fusion protein(s) comprising a repressor polypeptide that represses the activity of the reporter polypeptide **by conferring specific localization** in a cell such that the reporter polypeptide has reduced activity, wherein said reporter polypeptide is linked to the linker polypeptide, and **wherein cleavage** of said linker polypeptide at said protease cleavage site increases the activity of said reporter.

Claims 1-8, 57 and 58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-8, 57 and 58 are directed to all possible fusion proteins comprising a repressor polypeptide that represses the activity of the reporter polypeptide by conferring specific localization in a cell such that the reporter polypeptide has reduced activity, wherein said reporter polypeptide is linked to the linker polypeptide, and wherein cleavage of said linker polypeptide at said protease cleavage site increases the activity of said reporter. Specifically applicants claims are directed to those fusion proteins, such that the actual "cleavage event" at said protease cleavage site increases the activity of said reporter.

Applicants have failed to describe even a single species of those fusion proteins encompassed by the claimed fusion proteins such that the actual "cleavage event" at said protease cleavage site increases the activity of said reporter and the art does not teach such a fusion protein.

Further, applicants have not described those fusion proteins which comprise a reporter polypeptide which functions via the activity of the binding of an antibody to an epitope on the reporter polypeptide, wherein this activity is effected by the cellular localization of the reporter polypeptide. Applicants additional disclosure of reporters such as enzymes and fluorescent polypeptides is insufficient to adequately describe all polypeptides having an epitope that can be bound by an antibody or active antibody fragment.

Thus, the specification fails to describe any representative species and/or characteristics of those fusion proteins comprising a repressor polypeptide that represses the activity of the reporter polypeptide by conferring specific localization in a

cell such that the reporter polypeptide has reduced activity, wherein said reporter polypeptide is linked to the linker polypeptide, and wherein cleavage of said linker polypeptide at said protease cleavage site increases the activity of said reporter. As no predictability of structure is apparent for the claimed genus and given the lack of disclosed species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-8, 57 and 58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Applicants have given no guidance as to how make a fusion protein comprising a repressor polypeptide that represses the activity of the reporter polypeptide by conferring specific localization in a cell such that the reporter polypeptide has reduced activity, wherein said reporter polypeptide is linked to the linker polypeptide, and wherein cleavage of said linker polypeptide at said protease cleavage site increases the activity of said reporter. Specifically applicants have not given guidance as to how to make such a fusion protein, such that the actual "cleavage event" at said protease cleavage site increases the activity of said reporter. It is understood how a change in the cellular localization may result in a change in the activity of said reporter, but not the claimed cleavage event at said protease cleavage site and as this a limitation of the claimed fusion proteins, the claims are not enabled.

Those portions of claims 1-4, 7 and 58, drawn to any fusion protein comprising any reporter polypeptide that is a polypeptide having an epitope that can be bound by an antibody or active antibody fragment are further not enabled. Reporter polypeptides as so claimed, which are merely such reporters based on their presentation of an epitope, which can be bound by an antibody, are not described in the specification, nor is it clear how the localization of such a reporter's activity, which encompasses almost all polypeptides could be "activated" merely by its localization within the cell. For enzymes and transcriptional activators it is obvious that the presence of the enzymes or activators near their substrate is critical, so changing localization within the cell can obviously have an effect on the enzymes or activators activity. How does cellular localization alter antibody binding in a similar fashion?

Because of this lack of guidance, and the extended experimentation that would be required, it would require undue experimentation for one skilled in the art to make the claimed fusion proteins.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson, Ph.D.
Patent Examiner
Art Unit 1652
February 24, 2003